Original Article

Fentanyl versus nalbuphine for intubating conditions during awake fiberoptic bronchoscopy: A randomized double-blind comparative study

Sujata Chaudhary, Sachin Chaudhary, Mahendra Kumar, Rashmi Salhotra

Department of Anesthesiology, University College of Medical Sciences and Guru Teg Bahadur Hospital, Dilshad Garden, Delhi, India

Abstract

Background and Aims: Patient cooperation, sedation, anxiolysis, and topicalization are important prerequisites for the successful and safe conduct of awake intubation. Because of the pharmacological properties, opioids can facilitate this process. Fentanyl is an opioid agonist and nalbuphine is an agonist-antagonist. This study aims to compare these two opioids for their effect on sedation and intubating conditions during awake fiberoptic intubation.

Material and Methods: This randomized double-blind controlled study was conducted on 62 ASA I/II patients of either sex between the age of 20 and 60 years, weight between 40 and 80 kg, with MP class I/II airways requiring general anesthesia with endotracheal intubation. All patients received standard airway topicalization and nebulization. Patients were randomly allocated to one of the two groups according to a computer-generated random number table. Group F ($n = 31$) received fentanyl 2 μg/kg i.v. and group N ($n = 31$) received nalbuphine 0.2 mg/kg i.v. over 10 min before intubation. Fiberoptic intubation was attempted and lignocaine spray and propofol boluses were administered as and when required. Hemodynamic responses and intubating conditions were recorded. Repeated measure ANOVA, McNemar test, and Chi-square test or Fischer's exact test were used for data analysis. A $P < 0.05$ was considered significant.

Results: Cough score ($P = 0.458$), post-intubation score ($P = 1.000$), and sedation score ($P = 1.000$) were comparable among the two groups. Hemodynamic responses and propofol and lignocaine requirements were also comparable.

Conclusion: Both fentanyl and nalbuphine provide comparable intubating conditions when used before awake fiberoptic intubation with minimal adverse effects on hemodynamic profile.

Keywords: Airway management, difficult airway, fiberoptic, intubation

Introduction

Fiberoptic and video technologies are widely used during laryngoscopy for airway management. Awake fiberoptic intubation (AFOI) is the technique of choice in anticipated difficult airway situations. However, patients need to be prepared both psychologically and pharmacologically for cooperation and avoidance of violent withdrawal, vomiting or vigorous coughing, gagging, and glottic closure reflex during intubation.[1] Hemodynamic responses like increase in heart rate and blood pressure and desaturation can occur during AFOI, presenting challenges to the procedure.[2] Therefore, it is essential to prepare patient's airway for obtundation of airway reflexes, providing adequate sedation and anxiolysis without the loss of airway patency with preservation of adequate ventilation.

Address for correspondence: Dr. Rashmi Salhotra, A2/268, 2nd Floor, Paschim Vihar, New Delhi - 110 063, India.
E-mail: rashmichabra@yahoo.com

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Benzodiazepines, propofol, opioids, dexmedetomidine, etc., are some of the drugs used for this purpose. Propofol has rapid onset and offset of action with profound amnesia but is associated with apnea, hypotension, and pain on injection.[3] Fentanyl attenuates the hemodynamic response and discomfort during passage of the bronchoscope through vocal cords.[4] It has a rapid onset with a duration between 30 and 50 min. After fentanyl (2 to 4 μg/kg) i.v., the patient remains drowsy but conscious and cooperative. It may be associated with respiratory depression, nausea, vomiting, and itching during recovery.[5] Nalbuphine is an agonist-antagonist opioid. Because of its pharmacological properties, nalbuphine results in analgesia without respiratory depression, pruritus, and sedation[6,7] due to activation of supraspinal and spinal κ-receptor. It has been administered as an analgesic supplement for conscious sedation[7] or balanced anesthesia and as an analgesic for postoperative and chronic pain.[8]

At the time of planning of this research, nalbuphine had not been studied for intubating conditions during AFOI. Thus, the present study was aimed to compare fentanyl and nalbuphine for intubating conditions in terms of the level of sedation, cough score, tolerance to intubation, and hemodynamic responses during awake fiberoptic intubation. A requirement of supplemental propofol or lignocaine in addition to fentanyl or nalbuphine for facilitating endotracheal intubation and the incidence of side effects like hypoxia were also studied.

Material and Methods

This randomized double-blind controlled study was conducted between November 2015 and April 2017 in the Department of Anesthesiology and Critical Care at University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi, after obtaining approval from the Institutional Ethical Committee-Human Research (IEC-HR) (approval obtained in the meeting conducted on 21-10-15) and written informed consent from the participants. The study was registered with ctri.nic.in (Trial registration number CTRI/2018/02/011696).

Sixty-two ASA I/II patients of either sex, age between 20 and 60 years, weight between 40 and 80 kg, with MP class I/II airways requiring general anesthesia with endotracheal intubation were included. Patient refusing to participate or suffering from respiratory illnesses, those with known allergies to trial drugs, those undergoing emergency procedures, obstetric procedures, or on beta-blockers were excluded. Patients were randomly allocated to one of the two groups of 31 each, after shifting inside the OT, according to a computer-generated random number table. Group F patients received fentanyl 2 μg/kg body weight i.v. and group N patients received nalbuphine 0.2 mg/kg body weight i.v. The study drug was diluted in 20 ml normal saline and administered over a period of 10 min in both the groups. The study drug was prepared by an independent anesthesiologist not involved in the further conduct of the study. The nature of drug was unknown to the observer and the patient to ensure blinding.

All patients were kept nil per orally for 8–10 h prior to the procedure. Patients were premedicated with Tab Alprazolam 0.25 mg night before and morning of surgery. Tab Ondansetron 4 mg and Tab Ranitidine 150 mg were administered with sips of water 2 h before surgery.

In preoperative room, patency of both the nostrils was tested and the nostril with better patency was identified an iv line was secured. Topicalization was accomplished by nasal pledgets soaked in lidocaine with adrenaline solution (1 ml, 1%, 10 mg). Nebulization was done with 4% lignocaine 4 ml (160 mg) over 15 min. Xylometazoline nasal drops were instilled in both the nostrils. Pulse, blood pressure, and SpO_2 were recorded at baseline, before and after topicalization. Patients were then shifted to the OT table. Essential monitoring was instituted and all vital parameters such as HR, SBP, DBP, MAP, and SpO_2 were recorded.

Vital parameters were recorded before and after test drug infusion. Bronchoscope was prepared by lubrication with lignocaine jelly and an appropriately sized cuffed polyvinyl chloride endotracheal tube was loaded over it. Two puffs of 10% lignocaine (10 mg/puff) were used to anesthetize tongue and hypopharynx.

At the end of study drug infusion, sedation was evaluated by Ramsay sedation score (RSS) (1-Anxious, agitated, or restless, 2-Cooperative, oriented, or tranquil, 3-Sedated but responding to loud noise, 4-Asleep, brisk glabellar reflex, or response to loud noise, 5-Asleep, sluggish glabellar reflex, or response to loud noise, and 6-Asleep with no response to painful stimulus).[9] Bronchoscopy was attempted if RSS score of 2 was achieved. If RSS of 2 was not achieved with the test drug, propofol was administered in boluses of 2 ml (20 mg) till RSS of 2 was achieved. Once the RSS score ≥2 was achieved, bronchoscopy was performed through nasal approach from the more patent nostril. Oxygen was supplemented throughout the procedure through the other nasal cavity via a nasopharyngeal airway. Once the vocal cords were visualized, aliquots of 2 ml (40 mg) 2% lignocaine spray were administered to facilitate further advancement of bronchoscope till the carina was visualized. Tracheal tube was rail-roaded over the fiberscope. The fiberscope was then withdrawn and the placement of the tube was confirmed with

auscultation. General anesthesia was induced in accordance with the standard protocol and surgery was allowed to proceed.

Intubating conditions were evaluated in terms of cough score[10] (1-no cough; 2-slight cough, not >2 in sequence; 3-moderate cough, 3–5 in sequence; 4-severe cough, >5 in sequence) during bronchoscopy. Tolerance to intubation was evaluated by post-intubation score[11] determined after placement of the tube in the trachea (1-cooperative; 2-minimal resistance; 3-severe resistance).

Heart rate and saturation (SpO_2) were monitored continuously. HR, SBP, DBP, MAP, and SpO_2 were noted in preoperative period, before and after topicalization, before and after test drug, at the time of intubation, immediately after intubation, and 2, 5, 10, and 15 min after intubation. The total dose of lignocaine used as spray during bronchoscopy and propofol required during the entire procedure were recorded.

Sample size was calculated considering a cough score ≤2 and post-intubation score 1 for the fentanyl group in 10% patients according to a previous study[2] and assuming the same for nalbuphine group as 40%, a sample size of 31 subjects per group was sufficient with 80% power and 5% level of significance to detect the proportion in cough score and post-intubation score. Similarly, considering a sedation score to find a mean difference of 0.5 units among the two groups with standard deviation of 0.5 with power 80% and 5% level of significance, a sample size of 17 per group was sufficient. Taking the higher of the two values, a total of 62 patients with 31 in each group were studied.

Repeatedly measured parameters were compared using repeated measure ANOVA followed by Tukey's test. Paired qualitative data was compared by McNemar test and unpaired qualitative data was compared using Chi-square test or Fischer's exact test. A P value <0.05 was considered significant. All analysis was carried out in SPSS version 20.0.

Results

A total of 68 patients were assessed for eligibility. Six of these were excluded and finally, 62 patients were randomized and allocated to one of the two intervention groups. These patients completed the study procedure and were analyzed. [Figure 1]

The demographic profile of the two groups is shown in Table 1. Cough score, post-intubation score, and Ramsay sedation score are shown in Table 2.

Table 3 shows the Lignocaine 2% (2 ml bolus, 40 mg) and Propofol 1% (2 ml bolus, 20 mg) administered in each group to enhance patient comfort and facilitate endotracheal intubation. There was no significant difference between the two groups (P = 0.262 and 0.776, respectively).

Changes in heart rate recorded at various time intervals are shown in Figure 2 (P = 0.632). Mean systolic blood

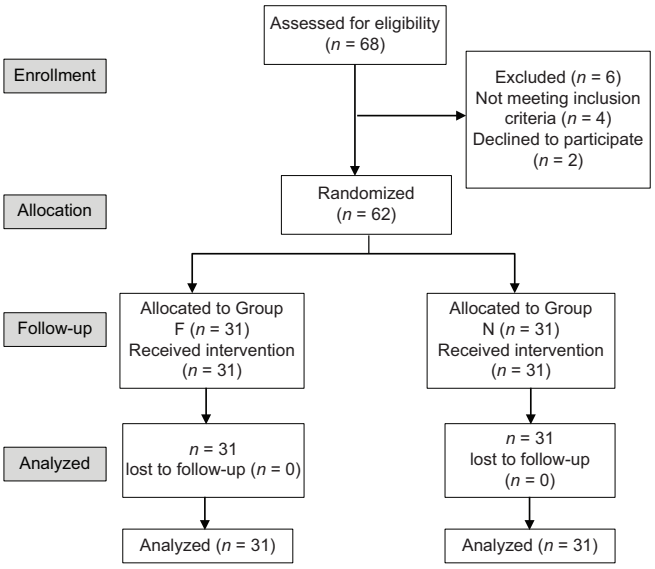

Figure 1: CONSORT flow diagram

Table 1: Demographic profile

Parameters	Group F (*n*=31)	Group N (*n*=31)	*P*
Age (years)	35.48±10.95	32.94±10.38	0.359 (NS)
Weight (kg)	63.52±8.02	63.68±7.45	0.935 (NS)
Height (cm)	161.39±6.93	160.87±6.88	0.770 (NS)
M:F	15:16	13:18	0.610 (NS)
ASA status I:II	23:8	27:4	0.199 (NS)
MP Class I:II	21:10	20:11	0.788 (NS)

P<0.05=significant. NS=nonsignificant

Table 2: Intubating conditions

Intubating conditions	Group F (*n*=31)	Group N (*n*=31)	*P*
Cough score			
1	0	2	0.458
2	26	23	
3	5	6	
4	0	0	
Post-intubation score			
1	0	0	1.000
2	31	31	
3	0	0	
Ramsay Sedation score (RSS)			
1	0	0	1.000
2	31	31	
3	0	0	
4	0	0	
5	0	0	
6	0	0	

P<0.05=significant

Table 3: Requirements of Lignocaine and Propofol boluses

No of boluses	Group F (*n*=31)	Group N (*n*=31)	*P*
Lignocaine 2% (2 ml, 40 mg)			
1	5	2	0.262
2	26	27	
3	0	2	
Propofol 1% (2 ml, 20 mg)			
1	4	3	0.776
2	25	27	
3	2	1	

Values are number of patients

pressure [Figure 3] was also comparable ($P = 0.710$). Mean diastolic blood pressure [Figure 3] was significantly less in group F compared to group N at 5 min post-intubation ($P = 0.042$). However, it remained comparable in both the groups at the rest of the time points. Mean blood pressure was comparable in both the groups at all the time points except at 2 min post-intubation, where it was significantly lower in group F compared to group N ($P = 0.011$).

There was no incidence of desaturation in any of the patients among the two groups. (Figure 4, $P = 0.357$).

Discussion

Awake fiberoptic intubation is required in many situations like anticipated difficult airway or cervical spine disorders. Patient cooperation is a big contributing factor for the success of the procedure along with psychological preparation, upper airway local anesthesia, and conscious sedation. In the present study, nasal packing, spraying, and nebulization with local anesthetic were done before intubation as a part of upper airway preparation. Following this, spraying of lidocaine was done once the vocal cords were visualized. This method was recommended by Sidhu *et al.* who found it to be safe, easy, and comfortable in a study on 58 patients.[12]

Fentanyl is used to provide conscious sedation[13] and attenuate hemodynamic response to endotracheal intubation. It has been used in a dose ranging between 1 and 8 μg/kg for the attenuation of intubation response in the previous studies. In a dose of 2 μg/kg, it was found to be effective for awake intubation[2] and for suppression of hemodynamic response to laryngoscopy and intubation.[4] Thus, in this study, we decided to use the same dose of fentanyl.

Nalbuphine has lesser potential for respiratory depression and is more cardiostable by virtue of it being a mixed agonist antagonist. Dhabhi *et al.*[14] and Nath *et al.*[15] have reported that nalbuphine is effective for the attenuation of hemodynamic

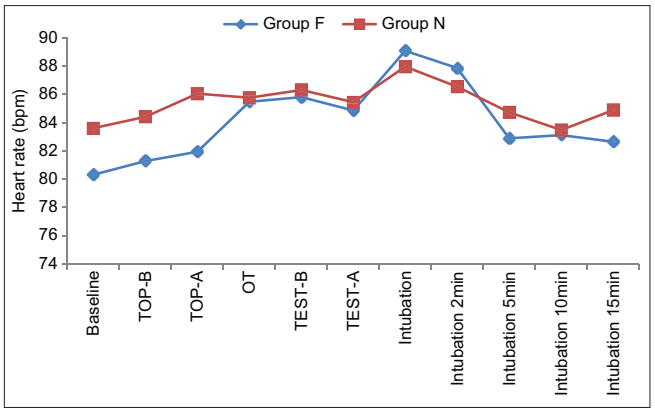

Figure 2: Mean heart rate at different time points

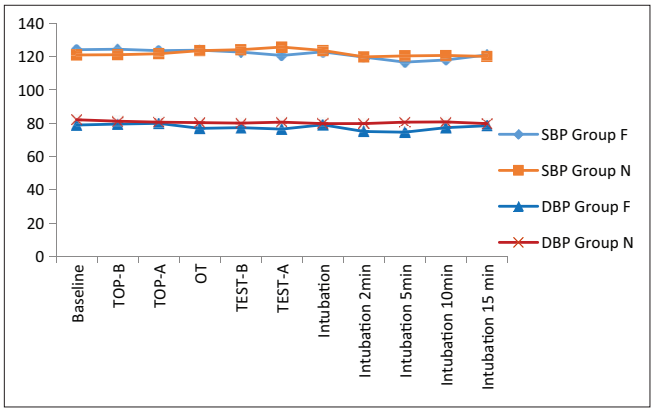

Figure 3: Mean systolic and diastolic blood pressure at different time points

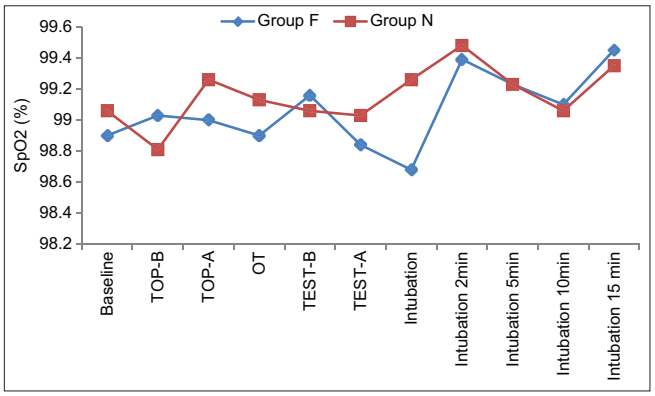

Figure 4: Oxygen saturation at different time points

response in a dose of 0.1 mg/kg and 0.2 mg/kg without any serious adverse effect. Considering the above fact, we decided to carry out our study with nalbuphine 0.2 mg/kg for AFOI.

In the study conducted by Mondal *et al.*[2] using dexmedetomidine 1 μg/kg or fentanyl 2 μg/kg for AFOI reported RSS to be 2.07 ± 0.25 in fentanyl group. In another study by Chaudhari *et al.*, nalbuphine 0.2 mg/kg was also reported to have RSS of 2.13 ± 0.48.[16] The sedation scores of these studies were similar to those of our study.

In the present study, cough score of 1 or 2 was achieved in most of the patients during AFOI and was comparable in both fentanyl and nalbuphine groups ($P = 0.458$). Mondal *et al.*[2] in their study reported a cough score of 3 with fentanyl, higher than that in our study. This may be because they used lower dose and concentration of 2% lignocaine (4 ml; 80 mg) for nebulization prior to AFOI compared to 4% lignocaine (4 ml; 160 mg) in our study. In addition, we also used aliquots of 2% lignocaine (2 ml; 40 mg) spray over the vocal cords.

The tolerance to intubation as graded on the post-intubation score was found to be 2 in all patients. Mondal *et al.*[2] reported a post-intubation score of ≥2 in 27 out of 30 patients in fentanyl group. The requirement of inj. lignocaine 2% and inj. Propofol 1% to facilitate trouble-free advancement of FOB in both the groups was comparable. Hence, both the drugs provided similar intubating conditions.

Studies done previously have reported that nalbuphine 0.2 mg/kg is effective in controlling hemodynamic response associated with direct laryngoscopy and oro-tracheal intubation.[14-16] Fentanyl 2 μg/kg was also effective in controlling hemodynamic response during awake fiberoptic bronchoscopy.[17] Similar findings were seen in our study also.

However, in our study, there was Mondal *et al.* reported significant desaturation ($SpO_2 \leq 94\%$) in fentanyl group as compared to dexmedetomidine group. They supplemented oxygen for the treatment of desaturation ($SpO_2 < 95\%$ for >10 s).[2] However in our study we did not find any episode of desaturation as the patients were provided oxygen through one of the nostrils throughout the procedure.

Our study has a few limitations. The patients included had normal airways belonging to MPG I and MPG II. Further studies are required to know the efficacy of nalbuphine and fentanyl for suppression of response to awake fiberoptic intubation in difficult airway.

From the above study, we conclude that both nalbuphine and fentanyl provide good intubating conditions with minimal adverse effects on hemodynamic profile of the patient for awake fiberoptic intubation. We recommend that fentanyl and nalbuphine both are efficacious and safe when used for awake fiberoptic intubation.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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